

Serial No. 09/748,739

Preliminary Amendment and Request for Continued Examination, filed Nov. 10, 2004

Remarks

Applicants cancel pending claims 3-39, inclusive, and amend Claims 1 and 2.

Applicants respectfully request that the amendments be entered.

The amendments are supported throughout the specification of the application as filed and add no substantive new matter. In particular, the basis for the language "comprising at least 95% sequence identity" in Claim 1 is found on page 10, lines 1 and 2. The basis for the language "to a sequence of amino acid residues 1 or about 29 through 602, inclusive, of amino acid sequence shown as SEQ ID NO:2" in Claim 1 is found in Figure 1. In that figure, the signal peptide is shown as amino acid residues -28 to -1, and the mature peptide begins at residue 1 and ends at residue 574. This same peptide is provided in the sequence listing as SEQ ID NO:2, with numbering from 1 to 602. The signal peptide of SEQ ID NO:2 (*i.e.*, residues 1 through 28) corresponds to residues -28 to -1 of Figure 2, and the mature peptide of SEQ ID NO:2 (*i.e.*, residues 29 through 602) corresponds to residues 1 through 574 of Figure 2. Claim 2 is amended by removal of the language "or functional fragment."

Applicants assert that these amendments provide the "structural metes and bounds" required to meet the written description requirement of 35 U.S.C. § 112, paragraph 1. Furthermore, these amendments limit the term "butyrylcholinesterase variant," providing definiteness and thereby meeting the requirements of section 112, paragraph 2.

The Examiner alleges that *no specific butyrylcholinesterase standard* is provided for measuring increased hydrolysis activity. Rejection, p. 5. Applicants respectfully argue that Example II, on pages 65-70 of the specification, teaches the use of *human wild-type butyrylcholinesterase* and *horse butyrylcholinesterase* as a reference in assays for the determination of increased hydrolysis activity in butyrylcholinesterase variants and thereby provides a specific standard.

The Examiner has stated a new rejection under 35 U.S.C. § 112, paragraph 2, because neither SEQ ID NO:2 nor SEQ ID NO:17 have Trp at position 328 of the sequence. Applicants point out that SEQ ID NO:17 is human wild-type butyrylcholinesterase (*see* Brief Description of the Drawings, p. 5 of the specification). As this sequence is not a variant, it does not contain the mutation A328W; instead, at position 328 it contains Ala, the wild-type residue. As for SEQ ID NO:2, as noted in the second paragraph of these remarks (above), SEQ ID NO:2 in the sequence listing contains the signal peptide, which is 28 residues long (*see* Figure 1 legend, point 2.) Using this reference, the skilled artisan would know that position 356 in the sequence listing SEQ ID NO:2 corresponds to residue 328 in the mature peptide (356 minus 28 residues of the signal peptide equals 328). This is readily apparent

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from the diagram in Figure 1, in which the signal peptide is numbered with negative numbers.

With respect to the provisional rejection for double patenting over co-pending application 10/032,233, Applicants agree to provide a terminal disclaimer in the later filed case if claims covering the same subject matter are allowed.

In view of the remarks and amendments provided herein, Applicants respectfully submit that all rejections have been addressed and request entry of the amendments, consideration of the arguments presented herein, and allowance of the claims. Applicants urge the Examiner to call the Applicants' agent at (317) 433-3422 if a telephone conversation or office interview would be helpful in expediting the prosecution of this case.

Respectfully submitted,

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